201-14404

Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

Ms. Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Dear Ms. Whitman:

CHEMICAL RIGHT TO KNOW – HPV CHALLENGE PROGRAM

On behalf of Dow AgroSciences LLC, I am please to submit the robust summaries in IUCLID format for Pentachloropyridine (Cas No.: 2176-62-7). As requested, the test plan has been posted onto the U.S. HPV Chemical Tracking System. All documents are in Adobe Acrobat (pdf) files.

We understand this information will be posted on the internet for comments for a period of 120 days. Please forward comments to me at the following address:

Ms. Gail M. Garvin
Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

Sincerely,

Gail M. Garvin
Global Environmental, Health & Safety Specialist
(317) 337-3609

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

201-14361A

TEST PLAN

For

2,3,4,5,6-PENTACHLOROPYRIDINE

Prepared by:

The Dow Chemical Company

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March 19, 2003

PLAIN ENGLISH SUMMARY

This test plan addresses 2,3,4,5,6-pentachloropyridine (CAS No. 2176-62-7). Existing data are summarized. Additional data will be collected under test plans under the HPV Challenge Program.

EXECUTIVE SUMMARY

The Dow Chemical Company hereby submits for review and public comment the test plan for 2,3,4,5,6-pentachloropyridine under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. It is the intent of The Dow Chemical Company to use new information in conjunction with a variety of existing data and scientific judgment/analyses to adequately characterize the SIDS (Screening Information Data Set) human health, environmental fate and effects, and physicochemical endpoints for this chemical.

Predictive computer models will be used to develop much of the environmental fate data for the chemical. The calculated data will be developed from a computer model used by the EPA. Physicochemical properties will be included.

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TEST PLAN FOR 2,3,4,5,6-PENTACHLOROPYRIDINE

I. INTRODUCTION

The Dow Chemical Company has committed voluntarily to develop screening level human health effects, environmental effects and fate, and physicochemical test data for 2,3,4,5,6-pentachloropyridine under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program (Program).

This plan identifies the chemical and its CAS number, identifies existing data of adequate quality for the chemical, and outlines testing planned to develop screening level data for the chemical under the Program. The objective of this effort is to identify and develop sufficient test data and/or other information to adequately characterize the human health and environmental fate for the chemical in compliance with the EPA HPV Program. Physicochemical data that are requested in this program will be provided.

II. DESCRIPTION OF 2,3,4,5,6-PENTACHLOROPYRIDINE

A. The Chemical

2,3,4,5,6-Pentachloropyridine (CAS No. 2176-62-7) is a member of a group of chemicals known as chloropyridines, used in the production of chlorinated pesticides. This material, like other structurally similar materials, has been studied to provide safe handling information.

III. TEST PLAN RATIONALE

A. Classification of the Chemical as a Production Chemical

Requirements

Classification of 2,3,4,5,6-pentachloropyridine is as a production chemical under the EPA HPV program.

B. Human Health Effects

There are six mammalian toxicity endpoints in the HPV Program:

Acute Toxicity
- Repeated Dose Toxicity
- Genetic Toxicity *In Vitro*
- Genetic Toxicity *In Vivo*
- Reproductive Toxicity

Developmental Toxicity

Published and unpublished data, as detailed in the attached Robust Summaries, satisfy the requirements of all required mammalian testing except Developmental Toxicity and Genetic Toxicity *In Vitro* and *In Vivo*. We propose to conduct tests for Developmental Toxicity (teratology study in rats), Genetic Toxicity *In Vitro* (Ames' test) as well as an In Vitro rat lymphocyte cytogenetics assay, as information from the EPA indicates that the combination of the two tests will satisfy requirements under the program. The attached Robust Summaries with the proposed testing provide adequate data to characterize the human health effects endpoints under the Program.

C. Ecotoxicity

There are three aquatic toxicity endpoints in the HPV Program:

- Acute Toxicity to Fish
- Acute Toxicity to Aquatic Invertebrates
- Toxicity to Algae (Growth Inhibition)

EPA identifies the following test methods to determine these endpoints: OECD Guideline 203, *Fish Acute Toxicity Test*; Guideline 202, *Daphnia sp., Acute Immobilization Test*; and Guideline 201, *Alga Growth Inhibition Test* [2] or equivalent studies.

Published and unpublished data, as detailed in the attached Robust Summaries, satisfies requirements for ecotoxicity data except for Toxicity to Algae. We propose to conduct a Toxicity to Algae (Growth Inhibition) study on *Selenastrum capricornutum*.

The existing data, along with the proposed testing, will be adequate to characterize ecotoxicity endpoints under the Program.

D. Environmental Fate

Predictive models were used to develop meaningful data for chemicals that are gaseous at relevant environmental temperatures and pressures. The environmental fate data include:

Photodegradation
- Stability in Water (Hydrolysis)
- Transport and Distribution (Fugacity)

- Biodegradation

1. Photodegradation

Photodegradation was estimated using models accepted by the EPA [4]. An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Chemicals that are gases will be available for atmospheric oxidation reactions with photochemically generated hydroxyl radicals. This will be the most significant route of degradation in the environment for category members.

The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) [1] is used by The Dow Chemical Company. This program calculates a chemical half-life based on an overall OH reaction rate constant, a 12-hr day, and a given OH concentration. This calculation was performed for 2,3,4,5,6-pentachloropyridine , as detailed in the attached Robust Summaries.

2. Stability in Water (Hydrolysis Modeling)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters [5]. However, halogenated aromatic organics are generally resistant to hydrolysis (Lyman, 1990). Stability in water can be measured [3] (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA [4]. An estimation method accepted by the EPA includes a model that can calculate hydrolysis rate constants for esters, carbamates, epoxides, halomethanes, and selected alkylhalides. The computer program HYDROWIN (aqueous hydrolysis rate program for Microsoft windows) [1] was used for hydrolysis calculation, as detailed in the attached Robust Summaries.

3. Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model [6]. EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* [4], which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent partitioned to 6 compartments within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for 2,3,4,5,6-pentachloropyridine. A computer model, EPIWIN - version 3.02 [1], will be used to calculate the properties needed to run the Level I EQC model.

4. Biodegradation Testing

Biodegradation is the utilization of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which are ultimately converted to an inorganic form such as carbon dioxide, nitrate, sulfate, and water. Assessing the biodegradability of organic chemicals using a standard testing guideline can provide useful information for evaluating chemical hazard.

Biodegradation values for 2,3,4,5,6-pentachloropyridine, as detailed in the attached Robust Summaries, were experimentally determined.

E. Physicochemical Properties

The physicochemical properties include:

- Melting Point
- Boiling Point
- Vapor Pressure
- Octanol/Water Partition Coefficient

Data for physicochemical properties will be summarized from various resources and detailed in the attached Robust Summaries.

IV. TEST PLAN SUMMARY

The following testing, modeling, and technical discussions will be developed for 2,3,4,5,6-pentachloropyridine:

- Conduct a teratology probe study and full study in rats
- Conduct an Ames study.

- Conduct an in vitro rat lymphocyte cytogenetics assay.
- Conduct an algal growth inhibition study on Selenastrum capricornutum. Calculate fugacity data.

Summaries of results will be developed once the data and analyses are available. This test plan is expected to provide adequate data to characterize the human health effects and environmental fate and effects endpoints under the Program.

For reasons indicated in the above paragraphs, we do not believe additional data needs to be generated beyond the studies listed. Due to the nature of the chemical; the manner in which the chemical is manufactured, distributed, processed and used, the product stewardship measures taken to prevent exposure; and existing human/environmental data, we believe that our workers, the public and the environment are well protected from exposure to PCP.

REFERENCES

1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.02. Syracuse Research Corporation, Syracuse, NY, USA.
2. Zepp, R. G., and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment. Environ. Sci. Technol. 11:359.366.
3. Howard, P. H. 1997. Handbook of Environmental Fate and Exposure Data. Vol. 5, pp. 196-200.
4. US EPA. 1999. Determining the Adequacy of Existing Data. OPPT, EPA.
5. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
6. Mackay, D., A. Di Guardo, S. Paterson, and C. E. Cowan. 1996. Evaluating the Environmental Fate of a Variety of Types of Chemicals Using the EQC Model. Environ. Toxicol. Chem. 15:1627-1637.
7. Lyman et al. 1990. Handbook of Chemical Property Estimation Methods.

201-14404B

IUCLID

Data Set

Existing Chemical	:	ID: 2176-62-7
CAS No.	:	2176-62-7
Common name	:	2,3,4,5,6-Pentachloropyridine

Producer Related Part

Company	:	The Dow Chemical Company
Creation date	:	20.05.2002

Substance Related Part

Company	:	The Dow Chemical Company
Creation date	:	20.05.2002
Memo		
Printing date	:	05.06.2002
Revision date		
Date of last Update	:	05.06.2002
Number of Pages	:	18
Chapter (profile)		
Reliability (profile)		
Flags (profile)	:	???

1.0.1 OECD AND COMPANY INFORMATION

Type
Name Dow AgroSciences
Partner
Date
Street 9330 Zionsville Road
Town Indianapolis, IN 46268-1189
Country United States
Phone
Telefax
Telex
Cedex
04.06.2002

Type :
Name : The Dow Chemical Company
Partner :
Date :
Street : 2020 Dow Center
Town : 48674 Midland, Michigan
Country : United States
Phone :
Telefax :
Telex :
Cedex :
20.05.2002

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant
Street
Town Freeport, TX
Country United States
Phone
Telefax
Telex
Cedex
04.06.2002

Name of Plant
Street
Town Pittsburg, CA
Country United States
Phone
Telefax
Telex
Cedex
04.06.2002

1.0.3 IDENTITY OF RECIPIENTS

Name of recipient The Dow Chemical Company
Street

Town	:	Freeport, TX
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	

04.06.2002

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	inorganic
Physical status	:	solid
Purity	:	> 99 % w/w
Test substance	:	Molecular formula = C5Cl5N Molecular weight = 251.3 Substance Type = organic Physical status = white solid Odor = sharp pyridine-like

04.06.2002

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

:Pentachloropyridine
20.05.2002

PCP
04.06.2002

1.3 IMPURITIES

CAS-No	:	
EINECS-No	:	
EINECS-Name	:	2,5,6-trichloro-3-pyridinecarboxylic acid
Contents	:	% w/w

04.06.2002

CAS-No	:	2808-86-8
EINECS-No	:	
EINECS-Name	:	Tetrachloropyridine
Contents	:	= .4 % w/w

04.06.2002

1.4 ADDITIVES

1.5 QUANTITY

Production during the

last 12 months
Import during the last 12 months
Quantity produced 10 - 50 tonnes in
04.06.2002

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

Type : type
Category : Non dispersive use
Remark : 1) 75 % used in the manufacturing of Symtet
2) 24.9 % sent to Freeport, Texas
3) 0.1% sent to external customers
04.06.2002

Type type
Category Use in closed system
04.06.2002

Type : industrial
Category : Agricultural industry
04.06.2002

Type : industrial
Category : other: pharmaceutical industry
04.06.2002

Type : use
Category : Intermediates
04.06.2002

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit other: Dow AgroSciences Industrial Hygiene Guide
Limit value 7 mg/m3
04.06.2002

1.9 SOURCE OF EXPOSURE

Memo Sources of Exposure
Remark Sampling conducted using Proper Protective Equipment per the MSDS recommendation.
This chemical is produced in Pittsburg, California and is shipped to Freeport, Texas. Therefore, chemical is present at two sites. The chemical known as PCP is an intermediate in the production of Symtet and Starane

Herbicide. Chlorine and Picolines are reacted in a vapor phase reactor followed by a series of liquid phase reactors. This material is then distilled with the PCP product stored in a tank prior to loading into a rail car. The unreacted material is recycled back to the reactors and reprocessed. The system is fully contained with no atmospheric vents. Vents are collected and sent to a vent condenser followed by thermal incineration or caustic scrubber. The scrubber effluent is sent to a Chlorinolysis facility for treatment and disposal. We have in process flow meters that perform material balances to ensure and track that PCP volumes do not escape into the environment. PCP is present in the Symtet intermediate at the 0.1 - 0.6 wt% level. PCP is not present in the end-use products of Garlon (Triclopyr) or Chlorpyrifos. PCP is also present in N-Serve 24 at the 0.2 - 0.44 wt% levels. This is an end use product.

04.06.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value	:	= 125 - 126 ° C
Sublimation	:	
Method	:	
Year	:	1982
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Measured value

04.06.2002 (1)

2.2 BOILING POINT

Value	:	= 273 ° C at
Decomposition	:	
Method	:	other: calculated
Year	:	2002
GLP	:	
Test substance	:	

04.06.2002 (2)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Decomposition		
Method		other (measured)
Year	:	1967
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	0.014 mm Hg at 25 0C

04.06.2002 (3)

2.5 PARTITION COEFFICIENT

Log pow	:	= 3.53 at ° C
Method		other (measured)
Year	:	1967
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

04.06.2002 (3)

2.6.1 WATER SOLUBILITY

Value	:	= 8.5 mg/l at 25 ° C
Qualitative	:	slightly soluble (0.1-100 mg/L)

Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other: measured
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Dissociation Constant: Not applicable. Does not ionize within environmentally relevant pH ranges.

04.06.2002 (4)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Indirect photolysis	
Sensitizer	OH
Conc. of sens.	1500000 molecule/cm3
Rate constant	= .000000000000011 cm3/(molecule*sec)
Degradation	ca. 50 % after 974 day
Source	The Dow Chemical Company, Midland, MI.

05.06.2002 (5)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

3.6 BOD5, COD OR BOD5/COD RATIO

COD		
Method	:	other: ThOD
Year	:	1975
GLP	:	no
COD	:	= .64 mg/g substance

04.06.2002 (6)

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	c = .47
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

04.06.2002 (7)

Type	:	static
Species	:	Notropis atherinoides
Exposure period	:	72 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
LC0	:	m = 1
LC50	:	c = 1.23
LC100	:	m = 2
Method	:	other
Year	:	1972
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Lake Emerald shiners were exposed to 1.0, 1.5, or 2.0 mg/L PCP for 72 hours in dechlorinated Lake Huron water at 50 deg. F. under static conditions.

04.06.2002 (8)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Species	:	other aquatic crustacea: sand shrimp
Exposure period	:	43 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC50	:	= 1.8
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

04.06.2002 (9)

Type	:	static
Species	:	other: ciliate protozoan, Tetrahymena pyriformis
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Method	:	
Year	:	1989
GLP	:	
Test substance	:	

04.06.2002 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	LD50
Species	rat
Strain	Fischer 344
Sex	male
Number of animals	12
Vehicle	other: corn oil
Value	= 435 mg/kg bw
Method	other
Year	1987
GLP	no
Test substance	as prescribed by 1.1 - 1.4
Method	Young adult male rats were fasted overnight. They were administered the material as a solution in corn oil at a dose volume of 10 ml/kg bw at dose levels of 100, 250, 500, or 750 mg/kg bw. Animals were observed closely for two weeks, then submitted for pathological examination. All animals which died prior to scheduled necropsy were also submitted for pathological examination. Body weights were recorded on the day of treatment (Study Day 0), and Study Days 1, 8, and 15.
Result	Acute oral toxicity was characterized as moderate. The acute oral LD50 for male rats was approximately 435 mg/kg, when calculated using the moving average method.

Dose (mg/kg)	Number Treated	Number Dead
100	3	0
250	3	0
500	3	2
750	3	3

In-life signs of toxicity were observed only in rats receiving 500 or 750 mg/kg, and included lethargy, tremors/muscle spasms, lacrimation, palpebral closure, and death on the day of treatment. No clinical evidence of treatment-related effects were seen at 100 or 250 mg/kg. All surviving rats gained weight over the 2-week observation period.

Source	The Dow Chemical Company, Midland, MI.
Reliability	(1) valid without restriction Study conducted in accordance with generally accepted scientific principles. GLP not compulsory at time study was performed.

05.06.2002

Type	:	LD50
Species	:	rat
Strain	:	no data
Sex	:	female
Number of animals	:	3
Vehicle	:	other: rodent chow
Value	:	= 126 - 1000 mg/kg bw
Method	:	other
Year	:	1963
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	The Dow Chemical Company, Midland, MI
Reliability	:	(2) valid with restrictions

05.06.2002

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	1
PDII	:	
Result	:	moderately irritating
EC classification	:	
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Neat Material: A male rabbit was prepared by shaving the hair from the entire abdomen with a straight razor and barber soap. The animal was then rested for several days to allow any abrasions to heal completely and to be sure skin was suitable for use. Two sites on the abdomen were used for applications: one intact, the other cross-hatched with a sharp hypodermic needle to penetrate the stratum corneum but not to produce more than a trace of bleeding. Ten applications were made to the intact abdominal site over a period of 14 days. Three consecutive daily applications were made to the abraded site. Both abdominal sites were covered with 1X1 cotton pads and held place with a single cotton cloth taped to remaining body hair. Applications were discontinued upon production of a substantial skin burn, or if the animal died. 10% Dilution in Dowanol* DPM: A male rabbit was prepared by shaving the hair from the entire abdomen with a straight razor and barber soap. The animal was then rested for several days to allow any abrasions to heal completely and to be sure skin was suitable for use. Ten applications (unoccluded) were made to the ear over a period of 14 days. Two sites on the abdomen were used for applications: one intact, the other cross-hatched with a sharp hypodermic needle to penetrate the stratum corneum but not to produce more than a trace of bleeding. Ten applications were made to the intact abdominal site over a period of 14 days. Three consecutive daily applications were made to the abraded site. Both abdominal sites were covered with 1X1 cotton pads and held place with a single cotton cloth taped to remaining body hair. Applications were discontinued upon production of a substantial skin burn, or if the animal died.
Result		Neat Material: At the intact abdominal site, slight to moderate hyperemia and slight edema was observed during the first week of application. Slight necrosis appeared after the 5th application. All signs of irritation resolved within 21 days. Similar results were seen at the abraded abdominal site, with the exception that necrosis was first observed after the 4th application. 10% Dilution in Dowanol* DPM: The site at the rabbit ear had no signs of irritation. Both the intact and abraded abdominal sites had slight to moderate hyperemia and edema appear within the first week. All signs of

irritation resolved within 21 days.

Source The Dow Chemical Company, Midland, MI.
05.06.2002

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure Time	:	24 hour(s)
Comment	:	
Number of animals	:	1
Result	:	not irritating
EC classification	:	not irritating
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Both eyes of a white rabbit were stained with 5% fluorescein dye and examined for evidence of injury or alterations. The rabbit was then allowed to rest for 24 hours before test. Two drops of the material were introduced into the right eye. The eye was washed within 30 seconds for 2 minutes in a flowing stream of tepid water. Two drops of material were introduced in a similar fashion to the left eye, but this eye was left unwashed. Immmediately after instillation into each eye, the rabbit was examined for signs of discomfort. Within 2-3 minutes after the unwashed eye was treated, each eye was observed for conjunctival and corneal response. Similar observations were made on both eyes at 1 hour, 24 hours, 48 hours, and 6-8 days post-treatment. Examinations were conducted both with and without fluorescein dye.
Result		In both washed and unwashed eyes, the material caused very slight discomfort and very slight conjunctival irritation which resolved within 1 hour.
Source		The Dow Chemical Company, Midland, MI.

05.06.2002 (13)

5.3 SENSITIZATION

Type	:	Split adjuvant test
Species	:	guinea pig
Concentration	:	Induction 5 % intracutaneous Challenge 5 % open epicutaneous
Number of animals	:	8
Vehicle	:	other: Dowanol* DPM/Tween* 80, 9/1
Result	:	sensitizing
Classification	:	
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	The Dow Chemical Company, Midland, MI.

05.06.2002

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatment	:	continuous
Post obs. period	:	none
Doses	:	0, 0.3, 1, 3, 10, 30 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	= 10 mg/kg bw
LOAEL	:	= 30 mg/kg bw
Method	:	other
Year	:	1968
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 10-15 45-day old rats/sex/dose group were treated with 0, 0.3, 1 3, 10, or 30 mg/kg/day via diet. Rats were randomly assigned to treatment groups. Vehicle for the test material and feed for the controls was Purina ground rodent chow. Diets designed to deliver the nominal dose were mixed weekly on the basis of rat body weight and feed consumption. Body weights and feed consumption were collected once/week for the duration of the study. All animals were observed frequently for clinical signs of toxicity. Blood samples were collected from 5 rats/sex/dose from the 0, 10, and 30 mg/kg/day levels via orbital sinus puncture during weeks 3 and 12, and at termination. Hematological parameters examined included Hgb, crit, RBC, WBC, and differential counts. Blood urea nitrogen determinations were run on 10 rats/sex/dose at termination, and SGPT determinations were run for 5 rats/sex/dose at 0 and 30 mg/kg/day levels on days 1, 3, 7, 14, 30, and termination (10 rats/sex/dose). A complete necropsy examination was conducted on a standard set of tissues, including reproductive organs. Weights were collected for lungs, heart, liver, kidneys, spleen, testes, and brain. In an effort to clarify testicular findings among dosed rats, additional studies were undertaken. Repeated intubation: Groups of 10 male rats/dose were given 0, 62.5, 125, or 250 mg/kg/day via gavage 5 days/week for 2 weeks. Rats were necropsied 3 and 18 days after the last dose Body weights and testicular weights were recorded, and testes, prostate, seminal vesicles, coagulating gland, and epididymis were examined for microscopic lesions. SGPT determinations were conducted at necropsy. Dietary: Groups of 30 male rats were given diets at dose levels of 0, 62.5, 125, or 250 mg/kg/day. 5 rats/dose were necropsied on test days 49, 119, 175, and 242. Body weights and testicular weights were recorded, and testes, prostate, seminal vesicles, coagulating gland, and epididymis were examined for microscopic lesions. Livers were also examined on rats killed on days 175 and 242. SGPT determinations were conducted at necropsy.
Result		There were no treatment-related morphological changes observed at any level in females. Male rats given 30 mg/kg/day had increased relative liver and kidney

weights and mild focal hyaline droplet degeneration of the convoluted tubules of the renal cortex. No histological changes were observed in livers.

Testicular tubal atrophy of varying degrees was observed at all dose levels in the male rats. Not all animals within a dose level were affected, and severity was not dose-related.

In the follow-up studies, no treatment-related differences were observed for final body weight, testicular weight, gross pathology and histopathology. There was a marked degeneration of SGPT values at all dose levels. In the repeated intubation experiment, values were moderately depressed 3 days after final dosing, but returned to normal by the 18 day kill. In the dietary experiment, SGPT values were severely depressed at 49 and 119 days. Values at 175 and 242 days improved, but were still markedly lower than controls. Testicular effects observed in the earlier study could not be replicated, even at these much higher dose levels.

Source The Dow Chemical Company, Midland, MI.
Reliability (2) valid with restrictions
05.06.2002 (14)

Species	:	rat
Sex	:	no data
Strain	:	other: Alderly Park
Route of admin.	:	inhalation
Exposure period	:	6 hours
Frequency of treatment	:	16 exposures
Post obs. period	:	none
Doses	:	saturated vapor; ~1 ppm (0.01 mg/L)
Control group	:	no data specified
NOAEL	:	= 1 ppm
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	no data
Result	:	No rats died, no toxic signs were observed, and no organs were affected at necropsy.
Source	:	The Dow Chemical Company, Midland, MI.
Reliability	:	(2) valid with restrictions

05.06.2002 (15)

5.5 GENETIC TOXICITY 'IN VITRO'

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

6. References

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7. Risk Assessment

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT